Determination of axillary metastasis by breast MRI after neoadjuvant chemotherapy in breast cancer

Breast mri after neoadjuvant chemotherapy

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Abstract

Aim: As a result of the developments in breast cancer treatment, the life expectancy of patients has been extended. This fact has brought the morbidity of breast cancer surgery to the fore. Axillary dissection is the major factor responsible for morbidity. In the present study, we aimed to determine the safety of sentinel node biopsy in patients without pathological lymph node involvement using breast MRI taken after neoadjuvant chemotherapy.

Material and Methods: The study was carried out in the General Surgery Department of Bagcilar Training and Research Hospital between 15.02.2021 and 15.07.2021 on patients planned to undergo surgery after neoadjuvant chemotherapy. Postoperative axillary pathology findings were compared with patients without pathological axillary lymphadenopathy in breast MRI results after neoadjuvant chemotherapy.

Results: Ninety patients were operated. After the treatment, 57 of them became cN0 on breast MRI. When ≥ 3 negative SLNB was removed in the group of patients who were cN0 after the treatment, no pathological lymph involvement was observed in the axilla.

Discussion: The gold standard for evaluating chemotherapy efficacy is pathologic assessment, the residual cancer burden score (RCB) and the Miller-Payne score are used for this purpose. However, these evaluations are not practical since they need the patient to undergo surgery. For this reason, imaging methods such as mammography, US, MRI and PET-CT are used in the follow-up of NACT treatment response. WHO criteria and RECIST are used to standardize treatment response values with imaging methods.

Keywords

Breast Cancer, Breast Mri, Complete Response, Neoadjuvant Chemotherapy, Sentinel Lymph Node Biopsy

Introduction

Breast cancer is the most common type of cancer which causes the most deaths among women in the world and in Turkey [1]. According to the 2020 data of the World Health Organization (WHO), breast cancer patients accounted for 11.7% of newly diagnosed cancer types in all ages and genders, and this number is 2,261,419 people annually. The widespread use of screening methods in developed countries has allowed breast cancer to be diagnosed at an early stage and potential treatment for the disease. In addition, continuously developing medical treatments reduce mortality due to breast cancer. The prolonged life expectancy has led to the questioning of the morbidities experienced by patients in the postoperative period and the improvement of quality of life has become increasingly prominent. The most important morbidity of breast cancer surgery is associated with surgical intervention on the axilla. In the current surgical approach, in patients who have not received preoperative chemotherapy and whose axilla is clinically and radiologically negative, sentinel lymph node biopsy (SLNB) instead of axillary dissection is unquestionably accepted. In patients undergoing neoadjuvant chemotherapy (NACT), the gold standard is still axillary dissection. Nevertheless, studies on the adaptation of SLNB to patients who have received NACT have been started, and many such studies have been published on how to evaluate the axilla accurately and reliably using various methods and lymph node detection agents.

This study was planned to investigate the answer to the question of whether the SLNB method with breast MRI taken after NACT could fully reflect the surgical staging of the axilla (low false negativity rate and high true positivity rate) in patients with locally advanced breast cancer.

Material and Methods

This study was conducted retrospectively with the participation of 90 patients who were diagnosed with locally advanced breast cancer between 15.02.2021 and 15.07.2021 at the General Surgery Clinic of Bagcilar Training and Research Hospital. The patients had been given neoadjuvant chemotherapy and subjected to re-staging with radiological controls based on breast MRI after the treatment. In all patients diagnosed with locally advanced breast cancer, breast staging is performed with MRI before and after NACT in our clinic in accordance with the guidelines. The age, demographic data, the Tru-cut pathology result of the breast and/or axillary mass before NACT, the number and the size (mm) of masses in the breast in the breast MRI taken after NACT and the status of the axilla (presence/absence of pathological LAP) were recorded by obtaining them from patient files in electronic environment. The cases that responded completely to the treatment based on physical examination and breast MRI performed after NACT were included in the study. Inclusion criteria: 1. Female patients older than 18 years of age who were T0-4, N1-3 and M0 according to the TNM system after clinical and radiological evaluation before NACT and who were diagnosed with primary invasive breast cancer based on Tru-cut biopsy, 2. The patients with a performance status of 0-1 according to Eastern Cooperative Oncology Group (ECOG), 3. Patients who received NACT treatment, 4. The patients with complete axillary response in the physical examination performed after NACT and on control breast MRI and who underwent surgical treatment.

The exclusion criteria for the study: 1. The patients who had previously undergone surgical treatment to the ipsilateral axillary area for any reason, 2. The patients with pathological axillary LAP or metastatic disease were observed in clinical examination and imaging methods after NACT, and 3. The patients with a history of allergy to isosulfan blue and/or indocyanine green.

A dual method (isosulfan blue (ISB) and indocyanine green (ICG)) was applied to determine sentinel lymph node (SLNB) in patients participating in the study. Axillary dissection, which is the standard treatment, was performed in patients who completed SLNB sampling, and the dissection material was sent in a separate container for pathological examination. It was aimed to remove at least two SLNBs with ISB and ICG. Both SLNB and axillary dissection material were sent to permanent pathology and the false negativity, false positivity, true negativity and true positivity rates of SLNB were calculated from the obtained data.

Statistical evaluation

Frequency and percentage values were presented for categorical variables. Mean, standard deviation, median, minimum and maximum values were presented for continuous variables. Chi-square analysis was performed for relationships between categorical variables. When appropriate, a single sample Chi-square was evaluated by Fisher's exact and Fisher Freeman Halton Test. The normality of the distribution was determined by Kolmogorov Smirnov Test. For variables that did not satisfy the normal distribution assumption, the Mann Whitney U test was used for two independent group comparisons and the Kruskal Wallis H test was used for more than two group comparisons. The Bonferroni-corrected Dunn Multiple Comparison test was used to determine the source of the significant difference in the Kruskal Wallis H test. The analyses were performed with SPSS 23 (Statistical Package for the Social Sciences) software. $p < 0.05$ was considered significant.

Ethical Approval

This study was approved by the Ethics Committee of Bagcilar Training and Research Hospital Clinical Research Ethics Committee (Date: 2021-03-02, No: 2021.01.1.04.004).

Results

Ninety patients with breast cancer who met the study criteria and received preoperative NACT were operated. SLN was not found in 10 patients. Thus, 80 patients were included in the study. The median age of the patients was 48 years (range: 29-79).

After physical examination and radiological imaging, it was found that the primary tumor was in the upper outer quadrant in 35 patients, in the upper inner quadrant in 15 patients, in the lower outer quadrant in 13 patients, in the lower inner quadrant in 7 patients, and in the retroareolar region in 10 patients. Tumor was single-focused in 58 patients, multicentric in 14 patients and multifocal in 8 patients. The mean size of primary masses on MRI was 21.8±12.05 mm, and the mean size of satellite lesion was 17.45±6.95 mm in 22 patients with satellite lesions. In the pre-NACT Tru-cut biopsy evaluation of

Table 1. Evaluation of patients without pathological lymph node involvement (cN0) on breast MRI after neoadjuvant chemotherapy

	Sentinel lymph node biopsy (SLNB)		Axillary lymph node	
	Number of patients (n)	Lymph node count (n)	Number of patients with axillary metastatic LN (n)	Number of patients with axillary non- metastatic LN (n)
	6	1 Negative	2	4
SLNB negative	11	2 Negative	2	9
	11	≥ 3 Negative	0	11
Total	28		4	24
	14	1 Negative	4	10
SLNB positive	7	2 Negative	3	4
	8	≥ 3 Negative	7	1
Total	29		14	15
Total	57		18	39

the patients, diagnosis was invasive ductal carcinoma in 75 patients, invasive lobular carcinoma in 4 patients, and invasive ductal carcinoma + invasive lobular carcinoma in 1 patient.

There were 57 patients who were evaluated as cN0 and had SLNB in radiological (breast MRI) evaluations after NACT. Dual method (ICG+ISB) was used to determine sentinel lymph nodes. All patients underwent axillary dissection after sentinel lymph node removal. SLNB was positive in 29 patients and negative in 28 patients. In the evaluation of SLNB negative patients, 2 of the 6 patients with one SLNB negative had metastatic nodule in axillary area and 2 of the 11 patients who had two SLNBs removed had additional metastatic lymph node while none of the 11 patients who had three or more SLNBs removed had additional metastatic lymph node. According to the results of this evaluation, when axillary cN0 was taken into account in breast MRI, the presence of ≥ 3 negative SLNB had a positive predictive value of 100% (Table 1).

Based on the evaluations, the sensitivity of the breast MRI taken after NACT for metastatic lymph node determination in the axillary region was 41.67% while the specificity was 95.45% and the accuracy was 71.25%.

Discussion

Breast cancer is the most common cancer with the highest death toll among women throughout the world [1]. Due to the advances in the diagnosis and treatment of breast cancer, its mortality has decreased considerably with a concomitant longer life expectancy [2]. This has brought to the fore the quality of life in patients after breast cancer surgery. The most important cause of morbidity after breast cancer surgery is the interventions made to axilla. Axillary involvement is the most important prognostic factor in determining the prognosis and treatment of breast cancer and recurrences occur most frequently [3]. For this reason, the question of how to evaluate and treat the axilla with the least intervention that would treat the axilla correctly without compromising the principles of oncological surgery has gained importance. In the 1990s, the lymph node in which cancer first metastasized in lymphatic spread was identified and it was shown that if there was no involvement in this lymph node, the tumor had not yet metastasized [4]. The lymph node where the tumor first metastasizes is called the "sentinel lymph node". Clinically, SLNB has been shown to be equivalent to axillary dissection in patients who are axillary lymph node negative. Thus, morbidities

such as lymphedema, seroma, numbness, wound infection, limitation of movement and chronic pain caused by axillary dissection could be minimized [5]. Therefore, NACT regimens were started to be applied to patients who were clinically axillary lymph node positive. As in early stage breast cancers, it was hypothesized that the axilla could be evaluated with SLNB in patients whose axilla became clinically negative, and studies were started on this issue. In the present study, it was aimed to find SLNB with the dual method (ICG+ISB) for the evaluation of the axilla in patients who did not have axillary pathological lymph nodes clinically and radiologically after NACT. According to the results of our study, it was observed that the negative SLNB ≥ 3 lymph node in patients who did not have pathological LAP in the axilla clinically and radiologically determined the absence of metastatic lymph nodes in the axillary area with a 100% accuracy. This is an important consideration for the evaluation of patients receiving NACT using SLNB instead of axillary dissection.

In breast cancer, NACT is preferred to treat nodal involvement in the axilla in order to both reduce and destroy the mass in the breast. If the chemotherapy regimen given is ineffective, the patient would be treated with an ineffective regimen again because the same regimen would be used both in breast cancer treatment and after surgery. Therefore, follow-up of the response after the chemotherapy regimen used has gained importance. The gold standard for evaluating chemotherapy efficacy is pathologic assessment, the residual cancer burden score (RCB) and the Miller-Payne score are used for this purpose [6]. However, these evaluations are not practical since they need the patient to undergo surgery. For this reason, imaging methods such as mammography, US, MRI and PET-CT are used in the follow-up of NACT treatment response. WHO criteria and RECIST are used to standardize treatment response values with imaging methods [7]. In our study, we used the Miller-Payne scoring system to evaluate the pathology response according to the RECIST criteria and to evaluate the radiological response. US is used in the evaluation of treatment response after NACT due to its advantages such as low cost, no radiation exposure, and ability to be performed on point of care basis. Conventional US has difficulty separating fibrotic and tumor tissues. Another disadvantage of the US in assessing the treatment response is that it depends on the experience of the person who performs NACT. Vriens et al. evaluated the response to NACT in 172 breast cancer patients and showed that US

measurements of the tumor tissue size were on the average 20% larger than they actually are [8] .Many studies showed that MRI exhibits higher accuracy in predicting the effectiveness of NACT [9].Although conventional US has low sensitivity in assessing the treatment response of NACT, new techniques such as electrography, CEUS (Contrast Enhanced Ultrasound using microbubbles) can improve US prediction accuracy [10]. In our study, we used breast MRI to evaluate the treatment response of NACT because of the low sensitivity of traditional US. Fibrous tissue has no vascularization whereas the tumor tissue has good vascularization. Since MRI is an imaging method that differentiates these two tissues efficiently, it is used to determine the size of fibrous tissue that develops in response to NACT and remaining tumor tissue. The NACT regimen may affect the evaluation of the MRI because drugs containing taxane and anthracycline have a greater antiangiogenic effect, which negatively affects the evaluation of MRI by disrupting vascularization [11]. In the presence of fibrosis and reactive inflammation around the tumor bed, MRI shows the residual disease larger size than it is. The presence of residual DCIS causes false positive diagnosis, while small residual lesion leads to a false negative diagnosis [12]. De Los Santos et al. found the accuracy of MRI to be 74% in predicting pCR (pathological complete response) [13]. Choi et al. found that in the evaluation of NACT treatment response, MRI had a sensitivity of 88.2%, a specificity of 62.5%, an accuracy of 75.7%, a PPV value of %71,4 and an NPV value of 83.3% [14]. In our study, we found that MRI had 47.7% sensitivity, 95.45% specificity, 88.24% PPV value and 66.67% NPV value in determining the axillary response. According to a meta-analysis by Liu et al., the sensitivity of PET/CT was 86% and the specificity of MRI was 88%, and they concluded that the combined use of these two imaging methods could provide better results in evaluating pCR after NACT [15]. In our study, we used MRI in the diagnosis and staging of pre-NACT breast cancer and in the evaluation of response to treatment after NACT. We found that the probability of metastatic lymph node in the axilla is low if ≥ 3 negative SLNB is performed in patients without pathological LAP in the axilla after NACT. We found that the radiological evaluation of the response to NACT, which was carried out in accordance with the literature, was consistent with the pathological assessment by the Miller-Payne system.

Limitation

The small number of patients in our study was the most important limitation.

Conclusıon

The most important cause of morbidity in locally advanced breast cancer patients is axillary dissection. When the axilla is cN0 based on breast MRI after NACT, SLNB can be performed instead of axillary dissection. Prospective randomized trials are needed in this regard.

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